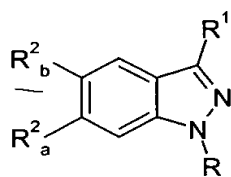
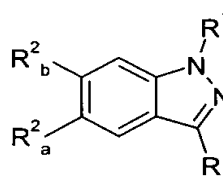


WHAT IS CLAIMED IS:

1. A method of treating or preventing stasis in all or any part or parts of the stomach of a patient in need of such treatment, wherein said stasis results from hypomotility in said stomach or part thereof, comprising administering to said patient a therapeutically effective amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme subtypes thereof, sufficient to restore normal motility to said patient, wherein said PDE4 inhibitor comprises a compound of Formula (IA) or (IB):



(IA)



(IB)

and to pharmaceutically acceptable salts thereof, wherein:

- R is a member independently selected from the group consisting essentially of hydrogen, (C₁-C₉) alkyl; -(CH₂)_n(C₃-C₁₀) cycloalkyl wherein n is an integer selected from 0, 1, and 2; (C₁-C₆) alkoxy(C₁-C₆) alkyl; (C₂-C₆) alkenyl; -(CH₂)_n(C₃-C₉) heterocyclyl wherein n is an integer selected from 0, 1, and 2; and -(Z¹)_b(Z²)_c(C₆-C₁₀) aryl wherein b and c are integers independently selected from 0 and 1, Z¹ is (C₁-C₆) alkylene or (C₂-C₆) alkenylene, and Z² is O, S, SO₂, or NR¹⁹; and further wherein said heterocyclyl is a member independently selected from the group consisting essentially of acridinyl; benzimidazolyl; benzodioxolane; 1,3-benzodioxol-5-yl; benzo[b]furanyl; benzo[b]thiophenyl; benzoxazolyl; benzthiazolyl; carbazolyl; cinnolinyl; 2,3-dihydrobenzofuranyl; 1,3-dioxane; 1,3-dioxolane; 1,3-dithiane; 1,3-dithiolane; furanyl; imidazolidinyl; imidazolyl; 1H-indazolyl; indolinyl; indolyl; 3H-indolyl; isoindolyl; isoquinolinyl; isothiazolyl; isoxazolyl; morpholinyl; 1,8-naphthyridinyl; oxadiazolyl; 1,3-oxathiolane; oxazolidinyl; oxazolyl; oxiranyl; parathiazinyl; phenazinyl; phenothiazinyl; phenoxazinyl; phthalazinyl; piperazinyl; piperidinyl; pteridinyl; pyranyl; pyrazinyl; pyrazolidinyl; pyrazolinyl; pyrazolo[1,5-c]triazinyl; pyrazolyl; pyridazinyl; pyridyl; pyrimidinyl; pyrimidyl; pyrrolyl; pyrrolidinyl; purinyl; quinazolinyl; quinolinyl; 4H-quinoliziny; quinoxaliny; tetrazolidinyl; tetrazolyl; thiadiazolyl; thiazolidinyl; thiazolyl; thienyl; thiomorpholinyl; triazinyl; and triazolyl; wherein said aryl is a carbocyclic moiety which is a member independently selected from the group consisting essentially of benzyl; *cis*- and *trans*-decahydronaphthalenyl; 2,3-1H-dihydroindenyl (indanyl); indenyl; 1-naphthalenyl; 2-

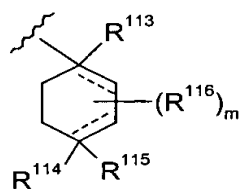
naphthalenyl; phenyl; and 1,2,3,4-tetrahydronaphthalenyl; wherein said alkyl, alkenyl, alkoxyalkyl, heterocyclyl, and aryl moieties defining said R groups are substituted by 0 to 3 substituents where each said substituent comprises a member independently selected from the group consisting essentially of bromo, chloro, or fluoro; hydroxy; (C₁-C₅) alkyl; (C₂-C₅) alkenyl; (C₁-C₅) alkoxy; (C₃-C₆) cycloalkoxy; mono-, di-, and tri-fluoromethyl; nitro; -C(=O)OR¹¹⁹, -C(=O)NR¹¹⁹R¹²⁰, -NR¹¹⁹R¹²⁰ and -S(=O)₂NR¹¹⁹R¹²⁰;

-R¹ is a member independently selected from the group consisting essentially of hydrogen; (C₁-C₉) alkyl; (C₂-C₃) alkenyl; phenyl; (C₃-C₇) cycloalkyl; and (C₃-C₇) cycloalkyl(C₁-C₂) alkyl; wherein said alkyl, alkenyl and phenyl moieties defining said R¹ groups are substituted by 0 to 3 substituents where each said substituent comprises a member independently selected from the group consisting essentially of methyl; ethyl; mono-, di-, and tri-fluoromethyl; and bromo, chloro, or fluoro; and

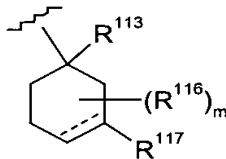
-R²_a and R²_b are independently selected from the group consisting essentially of hydrogen and hereinafter recited substituents, provided that one, but not both of R²_a and R²_b must be independently selected as hydrogen, wherein said substituents comprise moieties of the groups (- I -) through (- V -):

--(- I -)

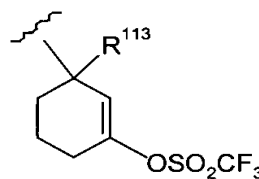
--a moiety of partial Formulas (1.0.0), (1.0.1), (1.0.2), and (1.0.3):



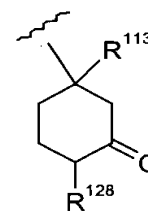
(1.0.0)



(1.0.1)



(1.0.2)



(1.0.3)

---wherein the dashed lines in partial Formulas (1.0.0) and (1.0.1) independently and optionally represent a single or double bond, provided that in formula (1.0.0) both dashed lines cannot both represent double bonds at the same time;

---m is an integer selected from 0, 1, 2, 3, and 4, and when 2, may apply to a single carbon atom on the ring;

---R¹¹³ is a member selected from the group consisting essentially of H; bromo, chloro, or fluoro; cyano; (C₂-C₄) alkynyl substituted by 0 or 1 substituent where said substituent is a member selected from the group consisting essentially of phenyl, pyridyl and pyrimidinyl; (C₁-C₄) alkyl substituted by 0 to 6 bromo, chloro, or fluoro; -CH₂NHC(=O)C(=O)NH₂;

cyclopropyl substituted by 0 or 1 substituent where said substituent is a member selected from the group consisting essentially of R^{121} ; R^{127} ; CH_2OR^{119} ; $NR^{119}R^{120}$; $CH_2NR^{119}R^{120}$; $C(=O)OR^{119}$; $C(=O)NR^{119}R^{120}$; $C\equiv CR_{11}$; $C(Z)H$; and $-CH=CR^{121}R^{121}$; provided that R^{113} is H in Formula (1.0.0) when the dashed line for the ring carbon of R^{113} attachment represents a double bond;

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--- R^{114} is a member selected from the group consisting essentially of H; R^{116} ; $C(Y)R^{124}$; $C(=O)OR^{124}$; $C(Y)NR^{127}R^{124}$; CN; $C(NR^{127})NR^{127}R^{124}$; $C(NOR^{119})R^{124}$; $C(=O)NR^{119}NR^{119}C(=O)R^{119}$; $C(=O)NR^{119}NR^{127}R^{124}$; $C(NOR^{124})R^{119}$; $C(NR^{119})NR^{127}R^{124}$; $C(NR^{124})NR^{119}R^{120}$; $C(NCN)NR^{127}R^{124}$; $C(NCN)S(C_1-C_4)$ alkyl; $CR^{119}R^{120}OR^{124}$; $CR^{119}R^{120}SR^{124}$; $CR^{119}R^{120}S(O)_nR^{125}$ where n is an integer selected from 0, 1, and 2; $CR^{119}R^{120}NR^{124}R^{127}$; $CR^{119}R^{120}NR^{127}S(=O)_2R_{15}$; $CR^{119}R^{120}NR^{127}C(Y)R^{124}$; $CR^{119}R^{120}NR^{127}C(=O)OR^{125}$; $CR^{119}R^{120}NR^{127}C(Y)NR^{127}R^{124}$; $CR^{119}R^{120}NR^{127}C(NCN)NR^{127}R^{124}$; $CR^{119}R^{120}NR^{127}C(CR^{119}NO_2)S(C_1-C_4)$ alkyl; $CR^{119}R^{120}C(=O)OR^{125}$; $CR^{119}R^{120}C(Y)NR^{127}R^{124}$; $CR^{119}R^{120}C(NR^{127})NR^{127}R^{124}$; $CR^{119}R^{120}CN$; $CR^{119}R^{120}C(NOR^{120})R^{124}$; $CR^{119}R^{120}C(NOR^{124})R^{120}$; $CR^{119}R^{120}NR^{127}C(NR^{127})S(C_1-C_4)$ alkyl; $CR^{119}R^{120}NR^{127}C(NR^{127})NR^{127}R^{124}$; $CR^{119}R^{120}NR^{127}C(=O)C(=O)NR^{127}R^{124}$; $CR^{119}R^{120}NR^{127}C(=O)C(=O)OR^{124}$; tetrazolyl; thiazolyl; imidazolyl; imidazolidinyl; pyrazolyl; thiazolidinyl; oxazolyl; oxazolidinyl; triazolyl; isoxazolyl; oxadiazolyl; thiadiazolyl; $CR^{119}R^{120}$ (tetrazolyl); $CR^{119}R^{120}$ (thiazolyl); $CR^{119}R^{120}$ (imidazolyl); $CR^{119}R^{120}$ (imidazolidinyl); $CR^{119}R^{120}$ (pyrazolyl); $CR^{119}R^{120}$ (thiazolidinyl); $CR^{119}R^{120}$ (oxazolyl); $CR^{119}R^{120}$ (oxazolidinyl); $CR^{119}R^{120}$ (triazolyl); $CR^{119}R^{120}$ (isoxazolyl); $CR^{119}R^{120}$ (oxadiazolyl); $CR^{119}R^{120}$ (thiadiazolyl); $CR^{119}R^{120}$ (morpholinyl); $CR^{119}R^{120}$ (piperidinyl); $CR^{119}R^{120}$ (piperazinyl); and $CR^{119}R^{120}$ (pyrrolyl); said heterocyclic groups being substituted by 0 to 3 substituents R^{124} ;

--- R^{115} is a member selected from the group consisting essentially of R^{119} ; OR^{119} ; $-CH_2OR^{119}$; cyano; $C(=O)R^{119}$; $C(=O)OR^{119}$; $C(=O)NR^{119}R^{120}$; and $NR^{119}R^{120}$; provided that R^{115} is absent when the dashed line in partial Formula (1.0.0) represents a double bond; or

--- R^{114} and R^{115} are taken together to form $=O$ or $=R^{118}$; or

--- R^{115} is hydrogen and R^{114} is OR^{124} ; SR^{124} ; $S(O)_nR^{125}$, where n is an integer selected from 0, 1, and 2; $S(=O)_2NR^{127}R^{124}$; $NR^{127}R^{124}$; $NR^{124}C(=O)R^{119}$; $NR^{127}C(Y)R^{124}$; $NR^{127}C(=O)OR^{125}$; $NR^{127}C(Y)NR^{127}R^{124}$; $NR^{127}S(=O)_2NR^{127}R^{124}$; $NR^{127}C(NCN)NR^{127}R^{124}$; $NR^{127}S(=O)_2R^{125}$; $NR^{127}C(CR^{119}NO_2)NR^{127}R^{124}$; $NR^{127}C(NCN)S(C_1-C_4)$ alkyl; $NR^{127}C(CR^{119}NO_2)S(C_1-C_4)$ alkyl; $NR^{127}C(NR^{127})NR^{127}R^{124}$; $NR^{127}C(=O)C(=O)NR^{127}R^{124}$; or $NR^{127}C(=O)C(=O)OR^{124}$;

---R¹¹⁷ is a member independently selected from the group consisting essentially of OR¹²⁴; SR¹²⁴; SO₂NR¹²⁷R¹²⁴; NR¹²⁷R¹²⁴; NR¹²⁴C(=O)R¹¹⁹; NR¹²⁷C(Y)R¹²⁴; NR¹²⁷C(=O)OR¹²⁵; S(O)_nR₁₂ where n is an integer selected from 0, 1, and 2; OS(=O)₂R¹²²; OR¹²²; OC(=O)NR¹²³R¹²²; OC(=O)R¹²³; OC(=O)OR¹²³; O(CR¹²²R¹²³)_mOR¹²² where m is an integer selected from 0, 1, and 2; CR¹¹⁹R¹²⁰OR¹²⁴; CR¹¹⁹R¹²⁰NR¹²⁷R¹²⁴; C(Y)R¹²⁴; C(=O)OR¹²⁴; C(Y)NR¹²⁷R¹²⁴; CN; C(NR¹²⁷)NR¹²⁷R¹²⁴; C(NOR¹¹⁹)R¹²⁴; C(=O)NR¹¹⁹NR¹¹⁹C(=O)R¹¹⁹; C(=O)NR¹¹⁹NR¹²⁷R¹²⁴; C(NOR¹²⁴)R¹¹⁹; C(NR¹¹⁹)NR¹²⁷R¹²⁴; C(NR¹²⁴)NR¹¹⁹R¹²⁰; C(NCN)NR¹²⁷R¹²⁴; C(NCN)S(C₁-C₄) alkyl; tetrazolyl; thiazolyl; imidazolyl; imidazolidinyl; pyrazolyl; thiazolidinyl; oxazolyl; oxazolidinyl; triazolyl; isoxazolyl; oxadiazolyl; and thiadiazolyl; where the recited heterocyclic groups are substituted by 0 to 3 substituents where said substituent is R¹²⁴;

---R¹¹⁹ and R¹²⁰ are each a member independently selected from the group consisting essentially of hydrogen and (C₁-C₄) alkyl substituted by 0 to 3 fluorine atoms;

---R¹²² is a member independently selected from the group consisting essentially of (C₁-C₆) alkyl; (C₂-C₃) alkenyl; (C₃-C₇) cycloalkyl; (C₃-C₇) cycloalkyl(C₁-C₂) alkyl; (C₆-C₁₀) aryl; and (C₃-C₉) heterocyclyl; where said aryl and heterocyclyl are as defined under R above; and where said R¹²² groups are substituted with 0 to 3 substituents independently selected from the group consisting essentially of methyl; ethyl; mono-, di-, and tri-fluoromethyl; and bromo, chloro, or fluoro;

---R¹²³ is a member independently selected from the group consisting essentially of hydrogen and R¹²²;

----R¹²⁴ is a member independently selected from the group consisting essentially of hydrogen and R¹²⁵, or when R¹²⁴ and R¹²⁷ appear together as NR¹²⁷R¹²⁴ then R¹²⁷ and R¹²⁴ may be taken together with the nitrogen to which they are attached to form a 5- to 7-membered ring optionally containing one additional heteroatom selected from O, N and S;

5 ----R¹²⁵ is a member independently selected from the group consisting essentially of (C₁-C₆) alkyl and -(CR¹¹⁹R¹²⁰)_nR¹²⁶, where n is an integer selected from 0, 1, and 2 and R¹²⁶ and said (C₁-C₆) alkyl are substituted by 0 to 3 substituents where each said substituent is a member independently selected from the group consisting essentially of bromo, chloro, or fluoro; nitro; cyano; NR¹²⁰R¹²⁷; C(=O)R¹¹⁹; OR¹¹⁹; C(=O)NR¹²⁰R¹²⁷; OC(=O)NR¹²⁰R¹²⁷; NR¹²⁷C(=O)NR¹²⁷R¹²⁰; NR¹²⁷C(=O)R¹²⁰; NR₁₇C(=O)O(C₁-C₄) alkyl; C(NR¹²⁷)NR¹²⁷R¹²⁰; C(NCN)NR¹²⁷R¹²⁰; C(NCN)S(C₁-C₄) alkyl; NR¹²⁷C(NCN)S(C₁-C₄) alkyl; NR¹²⁷C(NCN)NR¹²⁷R¹²⁰; NR¹²⁷S(=O)₂(C₁-C₄) alkyl; S(O)_n(C₁-C₄) alkyl; where n is an integer selected from 0, 1, and 2; NR¹²⁷C(=O)C(=O)NR¹²⁷R¹²⁰; NR¹²⁷C(=O)C(=O)R¹²⁷; thiazolyl; imidazolyl; oxazolyl; pyrazolyl; triazolyl; tetrazolyl; and (C₁-C₂) alkyl substituted with 0 to 3
15 fluorine atoms;

----R¹²⁶ is a member independently selected from the group consisting essentially of (C₃-C₇) cycloalkyl; pyridyl; pyrimidyl; pyrazolyl; imidazolyl; triazolyl; pyrrolyl; piperazinyl; piperidinyl; morpholinyl; furanyl; thienyl; thiazolyl; quinolinyl; naphthyl; and phenyl;

20 ----R¹²⁷ is a member independently selected from the group consisting essentially of OR¹¹⁹ and R¹²⁰;

----R¹²⁸ is a member independently selected from the group consisting essentially of H; C(Y)R¹²⁴; C(=O)OR¹²⁴; C(Y)NR¹²⁷R¹²⁴; CN; C(NR¹²⁷)NR¹²⁷R¹²⁴; C(NOR¹¹⁹)R¹²⁴; C(=O)NR¹¹⁹NR¹¹⁹C(=O)R¹¹⁹; C(=O)NR¹¹⁹NR¹²⁷R¹²⁴; C(NOR¹²⁴)R¹¹⁹; C(NR¹¹⁹)NR¹²⁷R¹²⁴; C(NR¹²⁴)NR¹¹⁹R¹²⁰; C(NCN)NR¹²⁷R¹²⁴; C(NCN)S(C₁-C₄) alkyl; CR¹¹⁹R¹²⁰OR¹²⁴; CR¹¹⁹R¹²⁰SR¹²⁴; CR¹¹⁹R¹²⁰S(O)_nR¹²⁵, where n is an integer selected from 0, 1, and 2; CR¹¹⁹R¹²⁰NR¹²⁴R¹²⁷; CR¹¹⁹R¹²⁰NR¹²⁷S(=O)₂R¹²⁵; CR¹¹⁹R¹²⁰NR¹²⁷C(Y)R¹²⁴; CR¹¹⁹R¹²⁰NR¹²⁷C(=O)OR¹²⁵; CR¹¹⁹R¹²⁰NR¹²⁷C(Y)NR¹²⁷R¹²⁴; CR¹¹⁹R¹²⁰NR¹²⁷C(NCN)NR¹²⁷R¹²⁴; CR¹¹⁹R¹²⁰NR¹²⁷C(CR₉NO₂)S(C₁-C₄) alkyl; tetrazolyl; thiazolyl; imidazolyl; imidazolidinyl; pyrazolyl; thiazolidinyl; oxazolyl; oxazolidinyl; triazolyl; isoxazolyl; oxadiazolyl; thiadiazolyl; wherein said recited heterocyclic groups are substituted by 0 to 3 substituents where each
25 said substituent is independently selected from the group consisting essentially of R¹²⁴;

----R¹²⁹ is a member independently selected from the group consisting essentially of -C(=O)R¹²; -C(=O)NR¹¹⁹R¹²⁴; -S(=O)₂R¹²⁵; and -S(=O)₂NR¹¹⁹R¹²⁴;

----Y is O or S; and,

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---Z is O; NR¹²⁷; NCN; C(-CN)₂; CR¹¹⁹CN; CR¹¹⁹NO₂; CR¹¹⁹C(=O)OR¹¹⁹; CR¹¹⁹C(=O)NR¹¹⁹R¹²⁰; C(-CN)C(=O)O(C₁-C₄) alkyl); and C(-CN)C(=O)NR¹¹⁹R¹²⁰;

- or, said substituents defining R²_a and R²_b comprise: -

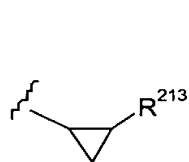
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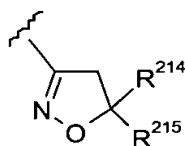
--a member selected from the group consisting essentially of R²²⁹,
 -C(=O)NR²²²(CHR²²²)_mC(=O)NR²²²O(CH₂)_q(C₆-C₁₀) aryl; -C(=NR²⁴²)NH(CH₂)_p(C₆-C₁₀) aryl;
 -C(=O)NR²¹⁸(CHR²²²)_mC(=O)NR²²²(CH₂)_pOR²²²; -C(=O)NR²²²(CHR²²²)_mS(C₁-C₄) alkyl;
 -C[=NOC(=O)R²³⁵]R²³⁶; -CR²²⁷R²²⁸CHR²³⁸NR²¹⁹SO₂(CH₂)_pA;
 -CR²²⁷R²²⁸CHR²³⁸NR²¹⁹P(=O)(OR²²²)C(=O)(C₁-C₄) alkyl;
 -CR²²⁷R²³⁸CHR²³⁸NR²¹⁹P(=O)[(C₁-C₄) alkoxy]₂, -Z³-R²¹⁷, and -(CR²²⁷R²²⁸)_mNR²¹⁹(C(O))_qR²²⁰
 wherein p is an integer selected from 0, 1, and 2; m is an integer selected from 1, 2, 3, 4, 5, and 6; and q is an integer selected from 1 and 2;

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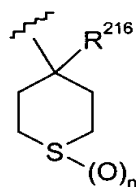
- or, said substituents defining R²_a and R²_b comprise a moiety of
 partial Formulas (2.0.0) through (2.0.8), inclusive: -



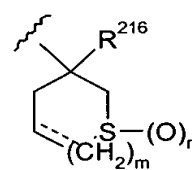
(2.0.0)



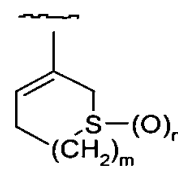
(2.0.1)



(2.0.2)

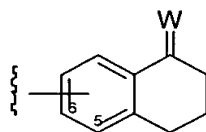


(2.0.3)

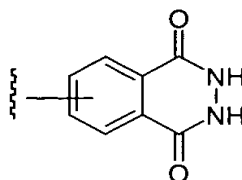


(2.0.4)

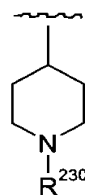
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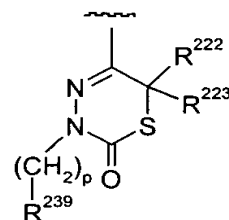
(2.0.5)



(2.0.6)



(2.0.7)



(2.0.8)

---wherein in said partial Formulas (2.0.0)-(2.0.8), the structures of partial Formulas (2.0.5) and (2.0.6) are attached to the nucleus of Formula (IA) or (IB) at carbons 5, 6, or 7 of said

partial Formulas (2.0.5) and (2.0.6); the dashed line in partial Formulas (2.0.2) and (2.0.3) indicates a single bond or double bond, except that R²¹⁶ is absent in partial Formulas (2.0.2) and (2.0.3) where said dashed line indicates a double bond; n is an integer selected from 0, 1, and 2; p is an integer selected from 0, 1, 2, 3, 4, 5, and 6; and m is an integer selected from 0, and 1;

---R²¹³ is a member independently selected from the group consisting essentially of -C(=O)N(CH₃)(OCH₃) and -(CH₂)_nOH, where n is an integer selected from 0, 1, 2, 3, and 4;

---R²¹⁴ and R²¹⁵ are independently selected from the group consisting essentially of H; ethyl; -CO₂H; and -C(=O)NHOH;

10 ---R²¹⁶ is a member independently selected from the group consisting essentially of H; hydroxy; (C₁-C₆) alkyl; (C₁-C₆) alkoxy; -OC(=O)(C₁-C₆) alkyl and -OC(=O)(C₆-C₁₀) aryl;

15 ----R²¹⁷ is a member independently selected from the group consisting essentially of (C₆-C₁₀) aryl and a 5- to 10-membered heterocyclyl, wherein said R²¹⁷ groups are substituted by 0 to 3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; trifluoromethyl; cyano; nitro; -CO₂R²²², (C₁-C₄) alkoxy; -OC(=O)(C₁-C₄) alkyl; -NR²²²C(=O)(C₁-C₄) alkyl; -C(=O)NH₂; -C(=O)NHOH; -C(=O)O(C₁-C₄) alkyl; (C₁-C₄) alkyl; -S(O)_nR²²² where n is an integer selected from 0, 1, and 2; benzoyl; -NR²²²R²²³, -OR²²², (C₁-C₆) alkanoyl; -Y¹-(C₆-C₁₀) aryl; -C(=O)O(C₆-C₁₀) aryl; -NH(C₆-C₁₀) aryl; -C(=O)NH(C₆-C₁₀) aryl; -C(=O)NR²²²O(CH₂)_n(C₆-C₁₀) aryl, where n is an integer selected from 1, 2, and 3; and -SO₂NH(C₆-C₁₀) aryl;

----R²¹⁸ is a member independently selected from the group consisting essentially of H; (C₁-C₆) alkyl; and -(CH₂)_n(C₆-C₁₀) aryl, where n is an integer selected from 0, 1, 2, 3, and 4;

----R²¹⁹ is a member independently selected from the group consisting essentially of H; -OR²²²; -(CH₂)_mA; and -CH₂O(CH₂)_mA, where m is an integer selected from 0, 1, and 2;

25 ----R²²⁰ is a member independently selected from the group consisting essentially of (C₁-C₄) alkyl; -OR²²², -CR²²²R²²³OR²²², -CR²²²R²²³NR²²²R²²³, -CR²²²(OR²²³)CR²²²R²²³OR²²², 2,2-dimethyl-1,3-dioxolan-4-yl; -NR²²²C(=O)NR²²²R²²³, -S(CR²²²R²²³)_nCH₃ where n is an integer selected from 0, 1, 2, 3, 4, and 5; -NR²²²(CH₂)_q(pyridyl) where q is an integer selected from 0 and 1; -P(=O)[(C₁-C₄) alkoxy]₂; -NR²²²R²²³, -NR²²²OR²²³, -NR²²²NR²²³R²²¹, -NR²²²CH₂R²²⁴, -OCH₂NR²²²C(=O)R²²⁴, -OCH₂C(=O)NR²²⁵R²²⁶, -OCHR²²²OC(=O)(C₁-C₄) alkyl; -OCHR²²²C(=O)(C₁-C₃) alkoxy; -O(CH₂)_mR²²¹; and -NR²²²(CH₂)_mR²²¹ where m is an integer selected from 0, 1, and 2;

---R²²¹ is a member independently selected from the group consisting essentially of H and A;

---R²²² and R²²³ are each a member independently selected from the group consisting essentially of H and (C₁-C₄) alkyl;

5 ---R²²⁴ is a member independently selected from the group consisting essentially of methyl and phenyl;

---R²²⁵ is a member independently selected from the group consisting essentially of H; methyl; ethyl; and -CH₂CH₂OH;

10 ---R²²⁶ is a member independently selected from the group consisting essentially of H; methyl; ethyl; -CH₂C(=O)NH₂; and -CH₂CH₂OH;

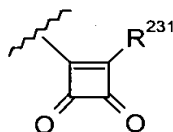
---R²²⁷ is each a member independently selected from the group consisting essentially of H; hydroxy; cyano; halo; (C₁-C₃) alkyl; (C₁-C₃) alkoxy; -NR²²²R²²³; -C(=O)OR²²²; -C(=O)R²²²; -CH=CR²²²R²²³; -C≡CR²²²; -CH₂NR²²²R²²³; -CH₂OR²²²; -C(=O)NR²²²R²²³; -C(Y⁵)H; and -CH₂NR₁₂C(=O)C(=O)NR²²²R²²³; provided that when R²²⁷ is hydroxy then R²²⁸ is H or (C₁-C₄) alkyl;

15 ---R²²⁸ is each a member independently selected from the group consisting essentially of H; fluoro; cyano; and (C₁-C₄) alkyl; where said methyl is substituted by 0 to 3 substituents each comprising a fluorine atom; or

---R²²⁷ and R²²⁸ are taken together to form an oxo (=O) moiety;

20 ---R²²⁹ is a member independently selected from the group consisting essentially of phenyl; naphthyl; pyrrolyl; furanyl; thienyl; oxazolyl; pyridinyl; pyrimidinyl; pyridazinyl; quinolinyl; isoquinolinyl; 5,6,7,8-tetrahydroquinolinyl; and 5,6,7,8-tetrahydroisoquinolinyl, where said R²²⁹ groups, except said phenyl, are substituted by 0 to 3 substituents R²³³, and wherein said phenyl R²²⁹ group is substituted by 0 to 3 substituents independently selected from R²³³ and R²³⁴;

25 ---R²³⁰ is a member independently selected from the group consisting essentially of -C(=O)R²³¹; -C(=O)C(=O)R²³¹; -C(=O)C(Y²)C(=O)R²³¹ and a moiety of partial Formula (2.0.9):



(2.0.9)

wherein:

- R²³¹ is a member independently selected from the group consisting essentially of H; -OR²³²; -NHR²³²; -NHOH; -NHNH₂; -(CH₂)_nY³(phenyl) and -(CH₂)_nY³(pyridyl) where n is an integer selected from 0, 1, 2, 3, and 4;
- 5 -----R²³² is a member independently selected from the group consisting essentially of H; (C₁-C₈) alkyl; -(CH₂)_nY³(phenyl) and -(CH₂)_nY³(pyridyl) where n is an integer selected from 0, 1, 2, 3, and 4;
- 10 -----R²³³ is each a member independently selected from the group consisting essentially of bromo, chloro, or fluoro; (C₁-C₆) alkyl; (C₁-C₇) alkoxy; (C₂-C₆) alkylendioxy; trifluoromethyl; -NR²²²R²²³; nitro; -C(NR²²²)NR²²²R²²³; -C(=O)NR²²²R²²³C(=O)R²²²; -C(NOR²²²)R²²³; -C(NCN)NR²²²R²²³; -C(NCN)SR²²²; -(CH₂)_m(CN) where m is an integer selected from 0, 1, 2, and 3; hydroxy; -C(=O)R²²²; -C(=O)NR²²²OR²²³; -C(=O)NR²²²NR²²²R²²³; -OC(=O)NR²²²R²²³; -NR²²²C(=O)R²²²; -C(=O)C(=O)NR²²²R²²³; -CO₂R²²²; -SO₂R²²²; -SO₂NR²²²R²²³; -C(=O)NR²²²R²²³; -NR²²²SO₂R²²³; and -NR²²²C(=O)NR²²²R²²³;
- 15 -----R²³⁴ is each a member independently selected from the group consisting essentially of imidazolyl; pyrazolyl; triazolyl; tetrazolyl; oxazolyl; isoxazolyl; oxadiazolyl; thiadiazolyl; thiazolyl; oxazolidinyl; thiazolidinyl; and imidazolidinyl, where each of said foregoing R²³⁴ substituents is substituted by 0 to 3 substituents R²³³;
- 20 -----R²³⁵ is a member independently selected from the group consisting essentially of -NR²²²R²²³; -NH(C₆-C₁₀) aryl; (C₁-C₆) alkoxy; and (C₆-C₁₀) aryloxy;
- R²³⁶ is a member independently selected from the group consisting essentially of H; (C₁-C₆) alkyl and -(CH₂)_mY⁴(phenyl) where m is an integer selected from 0, 1, 2, 3, and 4 and the phenyl moiety of said -(CH₂)_mY⁴(phenyl)R²³⁶ group is substituted by 0 to 3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; -OR²²²; (C₁-C₆) alkanoyloxy; (C₆-C₁₀) aryloxy; -NR²²²R²²³; -NH(C₆-C₁₀) aryl; and -NHC(=O)(C₁-C₄) alkyl;
- 25 -----R²³⁷ is each a member independently selected from the group consisting essentially of bromo, chloro, or fluoro; -(CH₂)_pNR²²²C(=O)CH₃ where p is an integer selected from 1, 2, 3, 4, and; (C₁-C₄) alkoxy; nitro; cyano; -NR²²²R²²³; -CO₂R²²²; -OR²²²; -C(Y¹)NR²²²R²²³; -NR²²²C(NCN)S(C₁-C₃) alkyl; -NR²²²C(NCN)NR²²²R²²³; -NR²²²C(=O)NR²²²R²²³; -NR²²²C(=O)C(=O)NR²²²R²²³; -C(=NR²²²)NR²²²R²²³; -S(O)_mCH₃ where m is an integer selected from 0, 1, and 2; -C(=NR²²²)S(C₁-C₃) alkyl; -NR²²²SO₂(C₁-C₃) alkyl; -OC(=O)R²²²;
- 30

$-\text{OC}(=\text{O})\text{NR}^{222}\text{R}^{223}$; $-\text{NR}^{222}\text{SO}_2\text{CF}_3$; $-\text{NR}^{222}\text{C}(=\text{O})\text{C}(=\text{O})\text{OR}^{222}$; $-\text{NR}^{222}\text{C}(=\text{O})\text{R}^{222}$;
 $-\text{NR}^{222}\text{C}(=\text{O})\text{OR}^{222}$; imidazolyl; thiazolyl; oxazolyl; pyrazolyl; triazolyl; and tetrazolyl;

5 $-----\text{R}^{238}$ is a member independently selected from the group consisting essentially of H; fluoro; cyano; and (C_1-C_2) alkyl, where said alkyl is substituted by 0 to 3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; $-\text{C}(=\text{O})\text{NR}^{222}\text{R}^{223}$; and $-\text{C}(=\text{O})\text{OR}^{222}$;

$-----\text{R}^{239}$ is a member independently selected from the group consisting essentially of phenyl substituted by 0 to 2 substituents independently selected from $-\text{NR}^{222}\text{R}^{223}$, nitro, halo, $-\text{OR}^{222}$, $-\text{NHR}^{240}$, $-\text{NR}^{240}\text{R}^{241}$, and $-\text{C}(=\text{O})\text{OR}^{222}$;

10 $-----\text{R}^{240}$ and R^{241} are each a member independently selected from the group consisting essentially of (C_1-C_8) alkyl and (C_2-C_8) alkenyl;

$-----\text{R}^{242}$ is pyridin-4-yl substituted by 0 to 2 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; and (C_1-C_4) alkyl;

15 $-----\text{A}$ is each a member independently selected from the group consisting essentially of (C_1-C_6) alkyl; pyridyl; morpholinyl; piperidinyl; imidazolyl; thienyl; pyrimidyl; thiazolyl; triazolyl; quinolinyl; phenyl; and naphthyl; wherein the foregoing A groups are substituted with 0 to 3 substituents R^{237} ; or A is $-(\text{CH}_2)_q\text{S}(\text{C}_1-\text{C}_4)$ alkyl wherein q is an integer selected from 1 and 2;

20 $-----\text{W}$ is a member independently selected from the group consisting essentially of O; NOH; NNH_2 ; $\text{NOC}(=\text{O})\text{CH}_3$; and $\text{NNHC}(=\text{O})\text{CH}_3$;

$-----\text{Y}^1$ is O or S;

$-----\text{Y}^2$ is O, NOH or H_2 ;

$-----\text{Y}^3$ is a bond or $-\text{CH}=\text{CH}-$;

$-----\text{Y}^4$ is a bond, O, S, or $-\text{NH}-$;

25 $-----\text{Y}^5$ is a member independently selected from the group consisting essentially of O; NR^{222} ; NOR^{222} ; NCN ; $\text{C}(\text{CN})_2$; $\text{CR}^{222}\text{NO}_2$; $\text{CR}^{222}\text{C}(=\text{O})\text{OR}^{222}$; $\text{CR}^{222}\text{C}(=\text{O})\text{NR}^{222}\text{R}^{223}$; $\text{C}(\text{CN})\text{NO}_2$; $\text{C}(\text{CN})\text{C}(=\text{O})\text{OR}^{222}$; and $\text{C}(\text{CN})\text{C}(=\text{O})\text{NR}^{222}\text{R}^{223}$; and

30 $-----\text{Z}^3$ is a member independently selected from the group consisting essentially of $-\text{NR}^{222}-$; $-(\text{CH}_2)_m-$; $-\text{CH}_2\text{C}(=\text{O})\text{NH}-$; $-\text{NHCH}_2\text{C}(=\text{O})-$; $-\text{CH}_2\text{C}(\text{Y}^1)\text{CH}_2-$; $-\text{CH}=\text{CH}-$; $-\text{C}\equiv\text{C}-$; $-\text{CH}(\text{Y}^1\text{H})-$; $-\text{C}(\text{Y}^1)-$; $-\text{CH}_2\text{C}(\text{Y}^1)-$; $-\text{C}(\text{Y}^1)\text{CH}_2-$; $-\text{C}(\text{Y}_1)\text{C}(\text{Y}_1)-$; $-\text{CH}_2\text{NR}^{222}-$; $-\text{CH}_2-\text{Y}^1-$; $-\text{C}(\text{Y}^1)\text{NR}^{218}(\text{CHR}^{222})_n-$; $-\text{NR}^{218}\text{C}(\text{Y}^1)(\text{CHR}^{222})_n-$; $-\text{NHCH}_2-$; $-\text{Y}^1-\text{CH}_2-$; $-\text{SOCH}_2-$; $-\text{CH}_2\text{SO}-$;

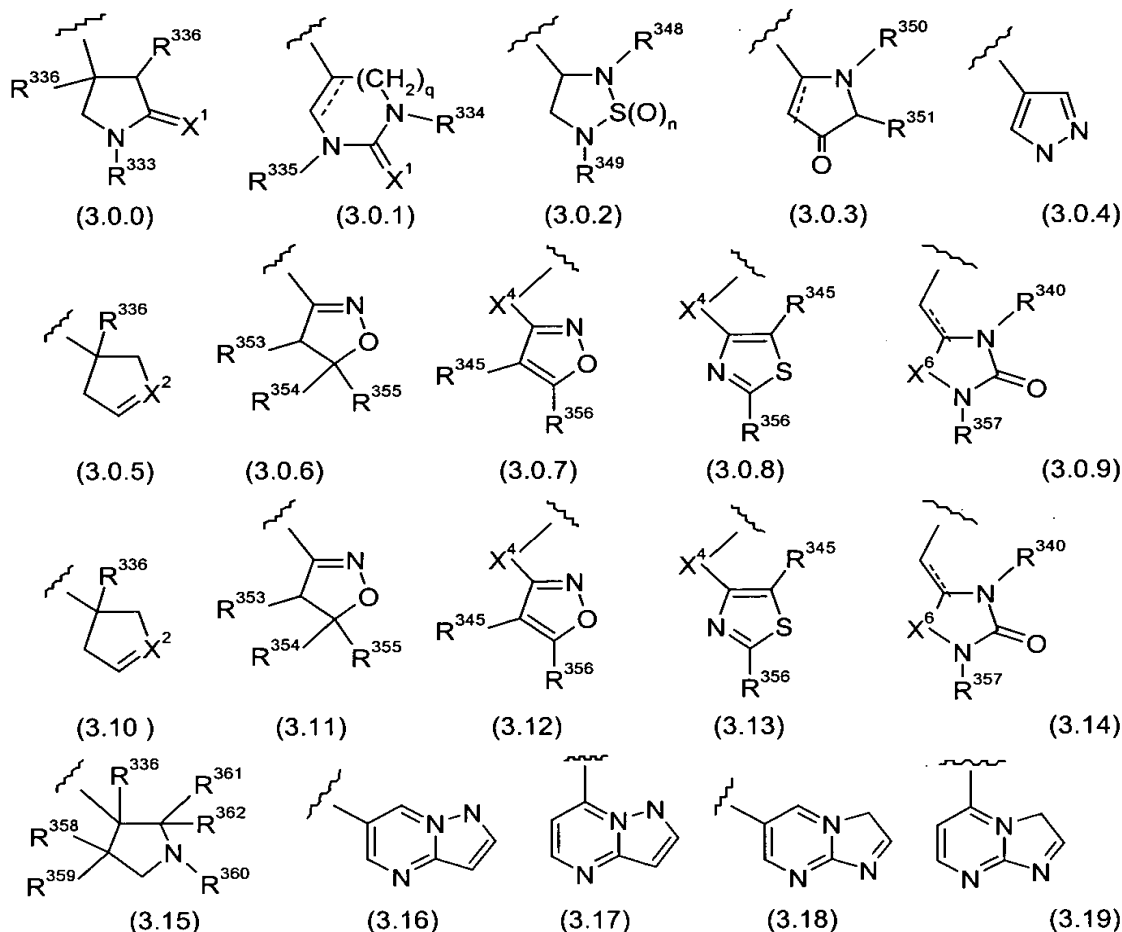
-SO₂CH₂-; -CH₂SO₂-; -OC(Y¹)-; -N=N-; -NHSO₂-; -SO₂NH-; -C(Y¹)C(Y¹)NH-; -NHC(=O)O-; -OC(=O)NH-; and -NHC(=O)NH-; wherein for said Z₃ moieties n is an integer selected from 0, 1, 2, 3, and 4; and m is an integer selected from 1, 2, and 3;

5 - or said substituents defining R²_a and R²_b comprise: -

--(- III -)

10 --a member independently selected from the group consisting essentially of 2-oxo-4-pyrrolyl; pyrazolyl; 2-oxo-3,4-dihydro-5-pyrimidyl; 2-oxo-3,4-dihydro-4-pyrimidyl; 2-oxo-tetrahydro-4-pyrimidyl; 2-oxo-tetrahydro-5-pyrimidyl; 2-oxo-4-pyrimidyl; and 2-oxo-5-pyrimidyl; wherein each of said R²_a and R²_b groups is substituted by 0, 1, 2, 3, or 4 R²³⁶ groups;

15 - or, said substituents defining R²_a and R²_b comprise a moiety of partial Formulas (3.0.0) through (3.0.19), inclusive: -



- wherein in said partial Formulas (3.0.0) through (3.0.19), q is an integer selected from 0 and 1 in partial Formula (3.0.1); n is an integer selected from 0, 1, and 2 in partial Formula (3.0.2); and the dashed lines appearing in formulas (3.0.1), (3.0.3), (3.0.6), (3.0.7), (3.0.8), (3.0.9) and (3.0.14) represent a double bond or a single bond;
- 5 -----X¹ is O or S;
- X² in formula (3.0.10) and where the dashed line in formula (3.0.9) represents a double bond, is a member independently selected from the group consisting essentially of CR³³⁵, CR³³⁶, CR³⁴⁶, and COC(=O)NR³³⁹R³⁴²; or, where the dashed line in formula (3.0.9) represents a single bond, X² is a member independently selected from the group consisting essentially of CR³³⁵R³³⁹, CR³³⁶R³³⁹, and CR³⁴⁶R³³⁹;
- 10 -----X³ is a member independently selected from the group consisting essentially of C(=Z³); C(S); and CR³³⁶R³⁴⁰;
- X⁴ is a member independently selected from the group consisting essentially of -(CH₂)_m, where m is an integer selected from 0, 1, and 2;
- 15 -----X⁵ is a bond or -CH₂-;
- X⁶ is a member independently selected from the group consisting essentially of -CH₂- and -C(=O)-;
- R³³³ is a member independently selected from the group consisting essentially of H; hydroxy; (C₁-C₄) alkoxy; -CHR³³⁷(O)_q(CH₂)_mA where q is an integer selected from 0 and 1, and m is an integer selected from 0, 1, and 2;
- 20 -----R³³⁴ is a member independently selected from the group consisting essentially of H; hydroxy; (C₁-C₄) alkyl; (C₁-C₂) alkoxy; -OC(=O)CH₃; (C₂-C₃) alkenyl; and phenyl(C₁-C₂) alkyl-;
- R³³⁵ is a member independently selected from the group consisting essentially of H; hydroxy; -(CH₂)_mA where m is an integer selected from 0, 1, and 2; (C₁-C₆) alkyl; and (C₂-C₃) alkanoyl; where said alkyl group is substituted by 0 to 3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; nitro; -NR³⁴⁰R³⁴¹; -CO₂R³⁴⁰; -OR³⁴⁰; -OC(=O)R³⁴⁰; -C(=O)R³⁴⁰; cyano; -C(=Y)NR³⁴⁰R³⁴¹; -NR³⁴⁰C(=Y)NR³⁴⁰R³⁴¹; -NR³⁴⁰C(=Y)R³⁴⁰; -NR³⁴⁰C(=O)OR³⁴⁰; -C(NR³⁴⁰)NR³⁴⁰R³⁴¹; -C(NCN)NR³⁴⁰R³⁴¹; -C(NCN)SR³⁴⁰; -NR³⁴⁰SO₂R³⁴⁰; -S(O)_mR³⁴⁰, where m is an integer selected from 0, 1, and 2; -NR³⁴⁰SO₂CF₃; -NR³⁴⁰C(=O)C(=O)NR³⁴⁰R³⁴¹; -NR³⁴⁰C(=O)C(=O)OR³⁴⁰; imidazolyl; and 1-(NHR³⁴⁰)-2-imidazolyl;
- 25
- 30

- R³³⁶ is each a member independently selected from the group consisting essentially of H; bromo, chloro, or fluoro; cyano; R³⁴³; cyclopropyl substituted by 0 or 1 substituent independently selected from the group consisting essentially of R³³⁹, -OR³⁴⁰, -CH₂OR³⁴⁰, -NR³⁴⁰R³⁴², -CH₂NR³⁴⁰R³⁴², -C(=O)OR³⁴⁰, -C(=O)NR³⁴⁰R³⁴², -CH=CR³³⁹R³³⁹, -C≡CR³³⁹, and -C(=Z³)H;
- R³³⁷ is a member independently selected from the group consisting essentially of H; -C(=O)R³³⁸; imidazolyl; pyrazolyl; triazolyl; tetrazolyl; oxazolyl; isoxazolyl; oxadiazolyl; thiadiazolyl; thiazolyl; oxazolidinyl; thiazolidinyl; and imidazolidinyl;
- R³³⁸ is each a member independently selected from the group consisting essentially of -OR³⁴⁰, -NR³⁴⁰R³⁴², and -R³⁴³;
- R³³⁹ is each a member independently selected from the group consisting essentially of H; bromo, chloro, or fluoro; and (C₁-C₄) alkyl substituted by 0 to 3 fluorine atoms;
- R³⁴⁰ and R³⁴¹ are each a member independently selected from the group consisting essentially of hydrogen and (C₁-C₄) alkyl;
- R³⁴² is each a member independently selected from the group consisting essentially of -OR³⁴⁰ and -R³⁴⁰;
- R³⁴³ is (C₁-C₄) alkyl;
- R³⁴⁴ is each a member independently selected from the group consisting essentially of bromo, chloro, or fluoro; nitro; cyano; -NR³⁴⁰R³⁴⁶, -NR³⁴⁶R³⁴², -C(=Z³)R³³⁸, -S(O)_mR³⁴³ where m is an integer selected from 0, 1, and 2; -OR³⁴²; -OC(=O)NR³⁴⁰R³⁴²; -C(NR³⁴²)NR³⁴⁰R³⁴²; -C(NR³⁴⁰)SR³⁴³; -OC(=O)CH₃; -C(NCN)NR³⁴⁰R³⁴²; -C(S)NR³⁴⁰R³⁴²; -NR³⁴²C(=O)R³⁴⁷; -C(=O)R³⁴⁷; oxazolyl; imidazolyl; thiazolyl; pyrazolyl; triazolyl; and tetrazolyl;
- R³⁴⁵ is each a member independently selected from the group consisting essentially of hydrogen and (C₁-C₄) alkyl substituted by 0 to 3 fluorine atoms;
- R³⁴⁶ is each a member independently selected from the group consisting essentially of H; -R³⁴³; -C(=O)R³⁴³; -C(=O)C(=O)R³³⁸; -C(=O)NR³⁴⁰R³⁴²; -S(O)_mR³⁴³ where m is an integer selected from 0, 1, and 2; -C(NCN)SR³⁴³; -C(NCN)R³⁴³; -C(NR³⁴²)R³⁴³; -C(NR³⁴²)SR³⁴³; and -C(NCN)NR³⁴⁰R³⁴²;
- R³⁴⁷ is each a member independently selected from the group consisting essentially of -R³⁴³; -C(=O)R³⁴³; oxazolidinyl; oxazolyl; thiazolyl; pyrazolyl; triazolyl; tetrazolyl; imidazolyl; imidazolidinyl; thiazolidinyl; isoxazolyl; oxadiazolyl; thiadiazolyl; morpholinyl;

piperidiny; piperaziny; and pyrroly; where each of said recited R^{347} heterocyclic groups is substituted by 0 to 2 (C_1 - C_2) alkyl groups;

----- R^{348} is each a member independently selected from the group consisting essentially of H; (C_1 - C_5) alkyl; (C_2 - C_5) alkenyl; benzyl; and phenethyl;

5 ----- R^{349} is a member independently selected from the group consisting essentially of H; (C_1 - C_5) alkyl; (C_1 - C_5) alkanoyl; and benzoyl;

----- R^{350} is a member independently selected from the group consisting essentially of H; (C_1 - C_4) alkyl; carboxy; aminocarbonyl; (C_1 - C_6) alkyl substituted by 0 or 1 carboxy, $-(CH_2)_mC(=O)(C_1-C_6)$ alkoxy; or $-(CH_2)_m(C_6-C_{10})$ aryl; where m is an integer selected from 0, 1, and 2;

----- R^{351} is a member independently selected from the group consisting essentially of H; (C_1 - C_6) alkyl; $-C(=Y)R^{352}$; $-C(=Y)NH_3$; $-C(=O)OR^{352}$; and $-(CH_2)_nX^7$ (pyridyl) where n is an integer selected from 0, 1, 2, 3, 4, and to 5; and X^7 is a bond or $-CH=CH-$; and where said pyridyl moiety is substituted by 0 or 1 bromo, chloro, or fluoro;

15 ----- R^{352} is a member independently selected from the group consisting essentially of (C_1 - C_6) alkyl (C_3 - C_8) cycloalkyl; $-(CH_2)_m(C_6-C_{10})$ aryl; and $-(CH_2)_nX^7$ (pyridyl) where n is an integer selected from 0, 1, 2, 3, 4, and 5; and X^7 is a bond or $-CH=CH-$; and where said pyridyl moiety is substituted by 0 or 1 bromo, chloro, or fluoro;

----- R^{353} is a member independently selected from the group consisting essentially of H; $-R^{345}$; (C_1 - C_3) alkyl substituted by 0 or 1 substituent hydroxy, or (C_1 - C_3) alkoxy(C_1 - C_3) alkyl;

----- R^{354} is a member independently selected from the group consisting essentially of H; $-R^{345}$; carboxy; (C_1 - C_3) alkoxy(C_1 - C_3) alkyl-; (C_3 - C_7) cycloalkyl; and (C_1 - C_5) alkyl substituted by 0 or 1 $-NR^{340}R^{341}$; or

25 ----- R^{353} and R^{354} are taken together to form $-CH_2OCH_2OCH_2-$;

----- R^{355} is a member independently selected from the group consisting essentially of H; hydroxy; (C_1 - C_4) alkyl substituted by 0 or 1 substituent comprising a member independently selected from the group consisting essentially of hydroxy; $-C(=O)R^{340}$; $-NR^{340}R^{341}$; $-(CH_2)_mNHC(=O)R^{340}$; $-(CH_2)_mNHC(=O)R^{343}$; $-(CH_2)_mCO_2R^{340}$; $-(CH_2)_mC(=O)NR^{340}R^{341}$; $-(CH_2)_mC(=O)N(OH)R^{340}$; $-(CH_2)_mSO_2NR^{340}R^{341}$; $-(CH_2)_mPO_3H_2$; $-(CH_2)_mSO_2NHC(=O)R^{343}$; and $-(CH_2)_mSO_2NHC(=O)(phenyl)$, where m is an integer selected from 0, 1, 2, 3, and 4;

-----R³⁵⁶ is a member independently selected from the group consisting essentially of H; (C₁-C₄) alkyl; phenyl; -NR³⁴⁰R³⁴¹; and -NR³⁴⁰(C₁-C₄) alkanoyl;

-----R³⁵⁷ is a member independently selected from the group consisting essentially of -R³⁴⁰; -CH₂CO₂R³⁴³; and -CH₂C(=O)NR³⁴⁰R³⁴¹;

5 -----R³⁵⁸ is a member independently selected from the group consisting essentially of -C(=O)R³⁴⁰; -C(=O)(C₆-C₁₀) aryl; -C(=O)(C₃-C₉) heteroaryl; -CO₂R³⁴⁰; -C(=O)NR³⁴⁰R³⁴¹; cyano; nitro; -CH₂OH; -NR³⁴⁰SO₂R³⁴⁰; -NHSO₂(C₆-C₁₀) aryl; -NHCO₂(C₁-C₄) alkyl; -NR³⁴⁰C(=O)R³⁴⁰; and -NHCO₂(C₆-C₁₀) aryl;

10 -----R³⁵⁹ is a member independently selected from the group consisting essentially of -R³⁴⁵; cyano; carboxy; formyl; -C(=O)R³⁴⁰; and (C₁-C₄) alkanoyl;

-----R³⁶⁰ is a member independently selected from the group consisting essentially of cyano; -NR³⁴⁰R³⁴¹; -SO₂(C₁-C₄) alkyl; -SO₂(C₆-C₁₀) aryl; -C(=O)R³⁴⁰; -C(=O)(C₆-C₁₀) aryl; -C(=O)(C₃-C₉) heteroaryl; -C(=O)NR³⁴⁰R³⁴¹; and -CO₂R³⁴⁰;

15 -----R³⁶¹ and R³⁶² are each a member independently selected from the group consisting essentially of H; cyano; nitro; -CO₂R³⁴⁰; -C(=O)NR³⁴⁰R³⁴¹; -CH₂OH; -C(=O)R³⁴⁰; -NHCO₂R³⁴⁰; and -NHSO₂R³⁴⁰;

20 -----A is a member independently selected from the group consisting essentially of pyridyl; morpholinyl; piperidiny; imidazolyl; thienyl; pyrimidyl; thiazolyl; phenyl; and naphthyl; where each of said A groups is substituted by 0 to 2 substituents R³⁴⁴ or by 1 substituent R³⁴⁵;

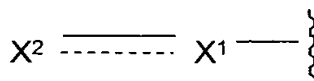
-----Z³ is a member independently selected from the group consisting essentially of O; -NR³⁴²; NOR³⁴⁰; N(CN); C(CN)₂; CR³⁴⁰NO₂; CR³⁴⁰C(=O)OR³⁴³; CR³⁴⁰C(=O)NR³⁴⁰R³⁴¹; C(CN)NO₂; C(CN)C(=O)OR³⁴³; and C(CN)C(=O)NR³⁴⁰R³⁴¹; and,

25 -----Y is O or S;

- or said substituents defining R²_a and R²_b comprise a moiety of partial Formula (4.0.0): -

-(- IV -)

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(4.0.0)

- wherein the broken line indicates a single or double bond;
- X¹ is -CR⁴⁷²R⁴⁷³- where said broken line indicates a single bond; or -CR⁴⁷³- where said broken line indicates a double bond;
- X² is -CR⁴⁷⁵R⁴⁷⁷R⁴⁷⁸- or -C(=NOR⁴⁸¹)R⁴⁸²- where said broken line indicates a single
5 bond; or -CR⁴⁷⁷R⁴⁷⁸ where said broken line indicates a double bond;
- R⁴⁷² is a member independently selected from the group consisting essentially of H; hydroxy; bromo, chloro, or fluoro; and -OR⁴⁷⁹;
- R⁴⁷³ is each a member independently selected from the group consisting essentially of
10 cyano; cyanomethyl; benzyloxy; -R⁴⁷⁵; -CO₂R⁴⁷⁵; -CO₂(CH₂)_n(C₆-C₁₀) aryl; -C(Y)NR⁴⁷⁵R⁴⁷⁶; -C(Y)NR⁴⁷⁵(CH₂)_n(C₆-C₁₀) aryl; -(CH₂)_n(C₆-C₁₀) aryl; and -(CH₂)_n(5- to 10-membered heteroaryl); where n is an integer selected from 0, 1, 2, and 3; each R⁴⁷³ group is substituted by 0 to 3 substituents R⁴⁷⁴; and each R⁴⁷³ group is substituted by 0 or 1 substituent R⁴⁸⁰;
- R⁴⁷⁴ is each a member independently selected from the group consisting essentially of
15 bromo, chloro, or fluoro; cyano; nitro; (C₁-C₆) alkyl; (C₂-C₆) alkenyl; -OR⁴⁷⁵; (C₃-C₇) cycloalkoxy; -NR⁴⁷⁵R⁴⁷⁶; -NR⁴⁷⁵OR⁴⁷⁶; -S(O)_mR⁴⁷⁵ where m is an integer selected from 0, 1, and 2; -CO₂R⁴⁷⁵; -C(=O)R⁴⁷⁵; -SO₂NR⁴⁷⁵R⁴⁷⁶; -C(=O)NR⁴⁷⁵R⁴⁷⁶; -CR⁴⁷⁵R⁴⁷⁶SO₂NR⁴⁷⁵R⁴⁷⁶; -CR⁴⁷⁵R⁴⁷⁶C(=O)NR⁴⁷⁵R⁴⁷⁶; -NHSO₂R⁴⁷⁵; -NHSO₂NR⁴⁷⁵R⁴⁷⁶; -NHC(=O)NR⁴⁷⁵R⁴⁷⁶; -NHC(=O)(C₁-C₆) alkyl; and -NHC(=O)O(C₁-C₆) alkyl);
- R⁴⁷⁵ and R⁴⁷⁶ are each a member independently selected from the group consisting
20 essentially of H; and (C₁-C₆) alkyl;
- R⁴⁷⁷ is a member independently selected from the group consisting essentially of -R⁴⁷³; 2-oxo-pyridyl; 3-oxo-pyridyl; 4-oxo-pyridyl; 2-oxo-pyrrolyl; 4-oxo-thiazolyl; 4-oxo-piperidyl; 2-oxo-quinolyl; 4-oxo-quinolyl; 1-oxo-isoquinolyl; 4-oxo-oxazolyl; 5-oxo-pyrazolyl; 5-oxo-isoxazolyl; and 4-oxo-isoxazolyl; where each of said R⁴⁷⁷ groups is substituted by 0 to 3
25 substituents R⁴⁷⁴;
- R⁴⁷⁸ is a member independently selected from the group consisting essentially of -R⁴⁷⁵; cyano; -(CH₂)_p(C₆-C₁₀) aryl; and -(CH₂)_p(5- to 10-membered heteroaryl); where p is an integer selected from 1, 2, and 3; and where each said R⁴⁷⁸ group is substituted by 0 to 3 substituents R⁴⁷⁴;
- R⁴⁷⁹ is a member independently selected from the group consisting essentially of formyl; carbamoyl; thiocarbamyl; (C₁-C₆) alkyl; (C₂-C₆) alkenyl; (C₁-C₄) alkoxy(C₁-C₄) alkyl-; and (C₁-C₆) alkanoyl; where said alkyl moieties of each of said R⁴⁷⁹ groups is substituted by 0 to

3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; hydroxy; and (C₁-C₄) alkoxy;

5 -----R⁴⁸⁰ is a member independently selected from the group consisting essentially of cyclobutyl; cyclopentyl; cyclohexyl; 2-cyclobuten-1-yl; 2-cyclopenten-1-yl; 3-cyclopenten-1-yl; 2,4-cyclopentadien-1-yl; 3,5-cyclohexadien-1-yl; pyrrolyl; pyrrolidinyl; dioxolanyl; imidazolyl; oxazolyl; imidazolidinyl; pyrazolyl; pyrazolidinyl; pyranyl; piperidinyl; 1,4-dioxanyl; morpholinyl; 1,4-dithianyl; thiomorpholinyl; piperazinyl; 1,3,5-trithianyl; oxazinyl; isoxazinyl; oxathiazinyl; and oxadiazinyl; where each of said R⁴⁸⁰ groups is substituted by 0 to 2 (C₁-C₂) alkyl;

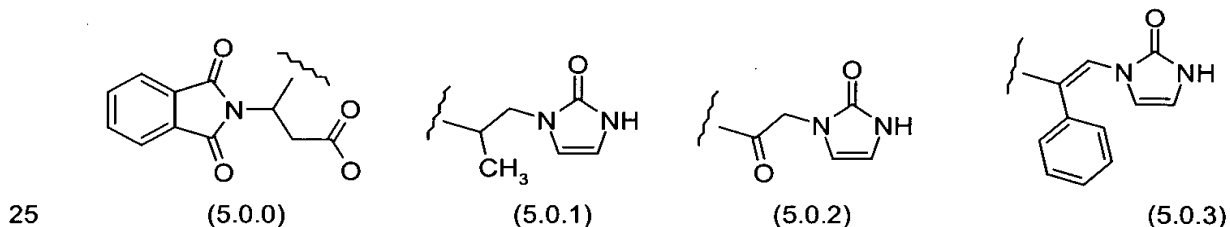
10 -----R⁴⁸¹ is a member independently selected from the group consisting essentially of H; (C₁-C₆) alkyl; (C₂-C₆) alkenyl; (C₂-C₆) alkynyl; -C(Y)NR⁴⁷⁵R⁴⁷⁶; -C(Y)NH(C₆-C₁₀) aryl; -C(Y)(C₁-C₆) alkoxy; -C(Y)(C₆-C₁₀) aryloxy; and -C(Y)(C₁-C₆) alkyl);

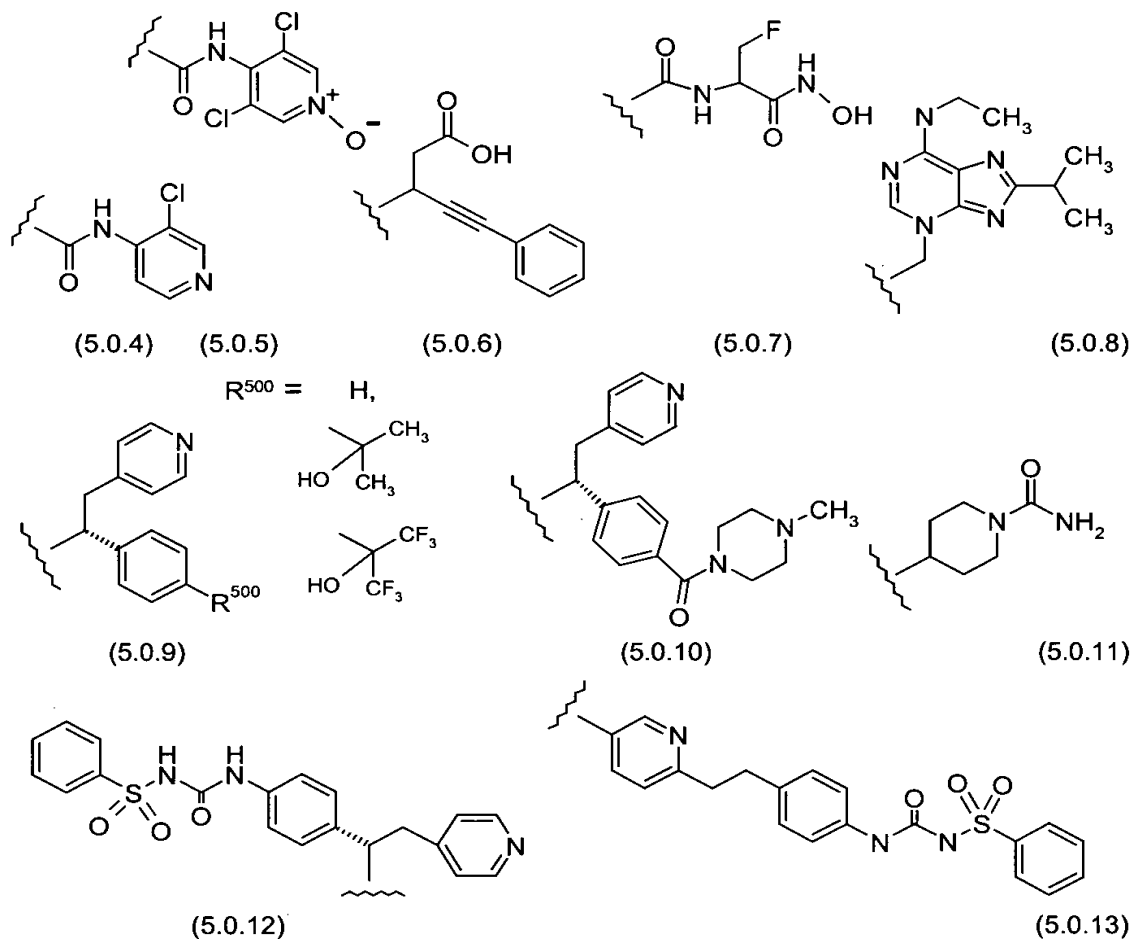
15 -----R⁴⁸² is a member independently selected from the group consisting essentially of phenyl and pyridinyl; where each of said R⁴⁸² groups is substituted by 0 to 3 substituents independently selected from the group consisting essentially of bromo, chloro, or fluoro; (C₁-C₄) alkyl; hydroxy; (C₁-C₄) alkoxy; -NR⁴⁷⁵R⁴⁷⁶; and -S(O)_mR⁴⁷⁵, where m is an integer selected from 0, 1, and 2; and,

-----Y is O or S;

20 - or , said substituents defining R²_a and R²_b comprise a moiety of partial Formulas (5.0.0) through (5.0.13), inclusive: -

--(- V -)





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2. A method according to Claim 1 wherein said stasis comprises gastric hypomotility with delayed emptying of the liquid and/or solid contents of the stomach of said patient being treated and said patient is a human.

3. A method according to Claim 2 wherein R^{2_a} and R^{2_b} are as defined under (- IV -) in Claim 1.

4. A method according to Claim 3 wherein R¹ is ethyl and R is cyclopentyl, cyclohexyl, or (C₆-C₁₀) aryl.

5. A method according to Claim 3 wherein R⁴⁷³ is -(CH₂)_n(C₆-C₁₀) aryl or -(CH₂)_n(5- to 10-membered heteroaryl), where n is an integer selected from 0, 1, 2, and 3.

6. A method according to Claim 5 wherein R⁴⁷³ is phenyl or pyridin-4-yl.

7. A method according to Claim 2 wherein R^{2_a} and R^{2_b} are as defined under (- I -) in Claim 1.

8. A method according to Claim 7 wherein R is cyclopentyl or cyclohexyl; R¹ is (C₁-C₂) alkyl; one of R^{2_a} and R^{2_b} is hydrogen and the other is a substituent of partial Formula (1.0.0) where the dashed line represents a single bond, m is 0, R¹¹³ and R¹¹⁴ are in a *cis* relationship to each other, R¹¹³ is cyano, R¹¹⁵ is hydrogen, and R¹¹⁴ is carboxy, -CH₂OH, or
5 -CH₂C(=O)NH₂.

9. A method according to Claim 7 wherein R is phenyl substituted by fluoro; R¹ is (C₁-C₂) alkyl; one of R^{2_a} and R^{2_b} is hydrogen and the other is a substituent of partial Formula (1.0.0) where the dashed line represents a single bond, R¹¹³ is cyano, and R¹¹⁵ and R¹¹⁴ are both hydrogen.

10 10. A method according to Claim 2 wherein said compound of Formula (IA) or (IB) as defined in Claim 1 is a member independently selected from the group consisting essentially of:

1-(1-Cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-oxocyclohexanecarbonitrile;

15 *Trans*-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Cis-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Trans-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Cis-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

20 1-(1-Cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-oxocyclohexanecarbonitrile;

Cis-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Trans-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

25 *Cis*-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Trans-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazole-6-yl)-4-hydroxymethylcyclohexanecarbonitrile;

Cis-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid amide;

Trans-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid amide;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-(1-hydroxy-1-methylethyl)cyclohexanecarbonitrile;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

Cis-1-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]-4-hydroxycyclohexanecarbonitrile;

5 *Cis*-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

Cis-1-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

Cis-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxy-4-methylcyclohexanecarbonitrile;

Trans-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxy-4-methylcyclohexanecarbonitrile;

Cis-4-cyano-4-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

10 *Trans*-4-cyano-4-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

6-Bromo-3-ethyl-1-(4-fluorophenyl)-1H-indazole;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]-4-hydroxycyclohexanecarboxylic acid ethyl ester;

15 4-Cyano-4-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohexanecarboxylic acid ethyl ester;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohex-3-enecarboxylic acid ethyl ester;

4-Cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-cyclohexanecarboxylic acid ethyl ester;

Cis-4-Cyano-4-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohexanecarboxylic acid;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohex-3-enecarboxylic acid; and

20 4-(1-Cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarboxylic acid.

11. A method of treating or preventing a gastric or gastrointestinal disorder in a mammalian patient in need of such treatment, wherein said gastric or gastrointestinal disorder is characterized by one or more symptoms selected from pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastroesophageal reflux, comprising administering to
25 said patient a therapeutically effective amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme subtypes thereof, sufficient to treat or prevent said gastric or gastrointestinal disorder in said patient, wherein said PDE4 inhibitor comprises a compound of Formula (IA) or (IB) as defined in Claim 1.

12. A method according to Claim 11 wherein R^2_a and R^2_b are as defined under
30 (- IV -) in Claim 1.

13. A method according to Claim 12 wherein R¹ is ethyl and R is cyclopentyl, cyclohexyl, or (C₆-C₁₀) aryl.

14. A method according to Claim 11 wherein R⁴⁷³ is -(CH₂)_n(C₆-C₁₀) aryl or -(CH₂)_n(5- to 10-membered heteroaryl), where n is an integer selected from 0, 1, 2, and 3.

5 15. A method according to Claim 14 wherein R⁴⁷³ is phenyl or pyridin-4-yl.

16. A method according to Claim 11 wherein R^{2_a} and R^{2_b} are as defined under (- I -) in Claim 1.

17. A method according to Claim 16 wherein R is cyclopentyl or cyclohexyl; R¹ is (C₁-C₂) alkyl; one of R^{2_a} and R^{2_b} is hydrogen and the other is a substituent of partial Formula
10 (1.0.0) where the dashed line represents a single bond, m is 0, R¹¹³ and R¹¹⁴ are in a *cis* relationship to each other, R¹¹³ is cyano, R¹¹⁵ is hydrogen, and R¹¹⁴ is carboxy, -CH₂OH, or -CH₂C(=O)NH₂.

18. A method according to Claim 16 wherein R is phenyl substituted by fluoro; R¹ is (C₁-C₂) alkyl; one of R^{2_a} and R^{2_b} is hydrogen and the other is a substituent of partial Formula
15 (1.0.0) where the dashed line represents a single bond, R¹¹³ is cyano, and R¹¹⁵ and R¹¹⁴ are both hydrogen.

19. A method of treating or preventing a gastric or gastrointestinal disorder in a mammalian patient in need of such treatment, wherein said gastric or gastrointestinal disorder is, with respect to said patient, (i) a sign or concomitant of diabetic neuropathy, anorexia
20 nervosa, achlorhydria, gastrointestinal surgery, post-surgical recovery in the period of emergence from general anesthesia; or the administration of morphine and morphine-like opioids; (ii) a secondary aspect of a primary disease or disorder in said patient which is organic, wherein said disease or disorder involves particularly a gastroenteric or gastroesophageal organ or tissue, or an organ or tissue of the central nervous system of said
25 patient; or (iii) an adverse side effect of a different therapeutic agent administered to said patient in the course of treating another unrelated disease or disorder in said patient, comprising administering to said patient a therapeutically effective amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme subtypes thereof, sufficient to treat or prevent said gastric or gastrointestinal disorder in said patient, wherein said PDE4 inhibitor
30 comprises a compound of Formula (IA) or (IB) as defined in Claim 1.

20. A method according to Claim 19 wherein said patient is a human.

21. A method according to Claim 20 wherein R^{2_a} and R^{2_b} are as defined under (- IV -) in Claim 1.

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B; α - and β -neoendorphin; [D-Ala²,MePhe⁴,Gly(ol)⁵]enkephalin (DAMGO); [D-Pen²,D-Pen⁵]enkephalin (DPDPE); [D-Ser²,Leu⁵]enkephalin-Thr⁶ (DSLET); [D-Ala²,D-Leu⁵]enkephalin (DADL); D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-NH₂ (CTOP); [D-Ala²,N-MePhe⁴,Met(O)⁵-ol]enkephalin (FK-33824); Tyr-D-Ala-Phe-Asp-Val-Val-Gly-NH₂ ([D-Ala²]deltorphan I; Tyr-D-Ala-Phe-Glu-Val-Val-Gly-NH₂ ([D-Ala²,Glu⁴]deltorphan II; Tyr-Pro-Phe-Pro-NH₂ (morphiceptin); Tyr-Pro-MePhe-D-Pro-NH₂ (PL-017); and [D-Ala²,Leu⁵,Cys⁶]enkephalin; (5) said leukotriene antagonist comprises a member independently selected from the group consisting essentially of ablukast; ablukast sodium; cinalukast; iralukast; montelukast sodium; ontazolast; pobelukast edamine; pranlukast; ritolukast; sulukast; tomelukast; verlukast; and zafirlukast; (6) said leukotriene biosynthesis (5-lipoxygenase) inhibitor comprises a member independently selected from the group consisting essentially of docebenone; enazadrem phosphate; and zileuton; (7) said thromboxane receptor antagonist comprises a member independently selected from the group consisting essentially of seratrovast; (8) said anticholinergic agent comprises a member independently selected from the group consisting essentially of ipratropium bromide; (9) said autocoid having agonist and antagonist activity useful for the treatment of pain and chronic inflammatory conditions, comprises a member independently selected from the group consisting essentially of bradykinin and kallidin; and their analogous derivatives independently selected from Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg (bradykinin); Lys-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg (kallidin); Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe (des-Arg⁹-bradykinin); Lys-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe (des-Arg¹⁰-kallidin); Arg-Pro-Pro-Gly-Phe-Ser-Pro-Leu (des-Arg⁹-[Leu⁸]-bradykinin); Arg-Pro-Pro-Gly-Phe-Ser-[D-Phe]-Phe-Arg ([D-Phe⁷]-bradykinin); and [D-Arg]-Arg-Pro-Hyp-Gly-Thi-Ser-Tic-Oic-Arg (HOE 140), where Hyp is *trans*-4-hydroxy-Pro; Thi is β -(2-thienyl)-Ala; Tic is [D]-1,2,3,4-tetrahydroquinolin-3-yl-carbonyl; and Oic is (3as,7as)-octahydroindol-2-yl-carbonyl; and (10) said cytokine is a member independently selected from the group consisting essentially of granulocyte colony-stimulating factor (G-CSF); granulocyte macrophage colony-stimulating factor (GM-CSF); and interleukin-1 (IL-1) through interleukin-12 (IL-12).

30. A pharmaceutical composition comprising a pharmaceutically acceptable carrier together with an amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme subtypes thereof, which is therapeutically sufficient to treat or prevent stasis in all or any part or parts of the stomach of a patient in need of such treatment, wherein said stasis results from hypomotility in said stomach or part thereof, and said amount is sufficient to restore normal motility to said patient; wherein said inhibitor of phosphodiesterase-4 (PDE4) comprises a compound of Formula (IA) or (IB) as defined in Claim 1.

31. A pharmaceutical composition according to Claim 30 wherein said patient is a human.

32. A pharmaceutical composition according to Claim 31 wherein R^2_a and R^2_b are as defined under (- IV -) in Claim 1.

5 33. A pharmaceutical composition according to Claim 32 wherein R^1 is ethyl and R is cyclopentyl, cyclohexyl, or (C₆-C₁₀) aryl.

34. A pharmaceutical composition according to Claim 31 wherein R^{473} is $-(CH_2)_n(C_6-C_{10})$ aryl or $-(CH_2)_n(5- \text{ to } 10\text{-membered heteroaryl})$, where n is an integer selected from 0, 1, 2, and 3.

10 35. A pharmaceutical composition according to Claim 34 wherein R^{473} is phenyl or pyridin-4-yl.

36. A pharmaceutical composition according to Claim 31 wherein R^2_a and R^2_b are as defined under (- I -) in Claim 1.

37. A pharmaceutical composition according to Claim 36 wherein R is cyclopentyl or cyclohexyl; R^1 is (C₁-C₂) alkyl; one of R^2_a and R^2_b is hydrogen and the other is a substituent of partial Formula (1.0.0) where the dashed line represents a single bond, m is 0, R^{113} and R^{114} are in a *cis* relationship to each other, R^{113} is cyano, R^{115} is hydrogen, and R^{114} is carboxy, -CH₂OH, or -CH₂C(=O)NH₂.

38. A pharmaceutical composition according to Claim 36 wherein R is phenyl substituted by fluoro; R^1 is (C₁-C₂) alkyl; one of R^2_a and R^2_b is hydrogen and the other is a substituent of partial Formula (1.0.0) where the dashed line represents a single bond, R^{113} is cyano, and R^{115} and R^{114} are both hydrogen.

39. A pharmaceutical composition according to Claim 30 wherein said compound of Formula (IA) or (IB) as defined in Claim 1 is a member independently selected from the group consisting essentially of:

1-(1-Cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-oxocyclohexanecarbonitrile;

Trans-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Cis-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Trans-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Cis-4-cyano-4-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

1-(1-Cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-oxocyclohexanecarbonitrile;

Cis-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

- 5 *Trans*-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid methyl ester;

Cis-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Trans-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazole-6-yl)-4-hydroxymethylcyclohexanecarbonitrile;

- 10 *Cis*-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid amide;

Trans-4-cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid amide;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-(1-hydroxy-1-methylethyl)cyclohexanecarbonitrile;

Cis-1-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

- 15 *Cis*-1-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]-4-hydroxycyclohexanecarbonitrile;

Cis-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

Cis-1-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarbonitrile;

Cis-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxy-4-methylcyclohexanecarbonitrile;

Trans-1-(1-cyclopentyl-3-ethyl-1H-indazol-6-yl)-4-hydroxy-4-methylcyclohexanecarbonitrile;

- 20 *Cis*-4-cyano-4-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

Trans-4-cyano-4-(1-cyclobutyl-3-ethyl-1H-indazol-6-yl)cyclohexanecarboxylic acid;

6-Bromo-3-ethyl-1-(4-fluorophenyl)-1H-indazole;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]-4-hydroxycyclohexanecarboxylic acid ethyl ester;

- 25 4-Cyano-4-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohexanecarboxylic acid ethyl ester;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohex-3-enecarboxylic acid ethyl ester;

4-Cyano-4-(1-cyclohexyl-3-ethyl-1H-indazol-6-yl)-cyclohexanecarboxylic acid ethyl ester;

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Cis-4-Cyano-4-[3-ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohexanecarboxylic acid;

4-[3-Ethyl-1-(4-fluorophenyl)-1H-indazol-6-yl]cyclohex-3-enecarboxylic acid; and

4-(1-Cyclohexyl-3-ethyl-1H-indazol-6-yl)-4-hydroxycyclohexanecarboxylic acid.

40. A pharmaceutical composition comprising (i) a pharmaceutically acceptable
5 carrier; (ii) an amount of an inhibitor of phosphodiesterase-4 (PDE4), including isozyme
subtypes thereof, which is therapeutically sufficient to treat or prevent stasis in all or any part
or parts of the stomach of a patient in need of such treatment, wherein said stasis results from
hypomotility in said stomach or part thereof caused by a therapeutic agent which causes or is
known to cause gastric hypomotility or related gastric or gastrointestinal disorders when
10 administered to said patient in therapeutically effective amounts, wherein said inhibitor of
phosphodiesterase-4 (PDE4) comprises a compound of Formula (IA) or (IB) as defined in
Claim 1; and (iii) a therapeutic agent which causes or is known to cause gastric hypomotility
or related gastric or gastrointestinal disorders when administered to said patient in
therapeutically effective amounts, wherein said therapeutic agent comprises one or more
15 members independently selected from the group consisting essentially of analgesics acting by
inhibition of prostaglandin synthesis; antacids which contain calcium carbonate or aluminum
hydroxide; anticholinergic agents; antidiarrheal agents; antihistamines which are H₁ blockers
or have an anticholinergic effect; antiparkinsonian drugs which have an anticholinergic effect;
barium sulfate; corticosteroids; clonidine; diuretics which cause hypokalemia; ganglionic
20 blocking agents; heavy metals; laxatives; lithium; monoamine oxidase inhibitors; muscle
relaxants; octreotide; opioids; phenothiazines having an anticholinergic effect; polystyrene
resins; propranolol; tricyclic antidepressants having an anticholinergic effect; and verapamil.

41. A pharmaceutical composition according to Claim 40 wherein said analgesics
acting by inhibition of prostaglandin synthesis comprise NSAIDs; said heavy metals comprise
25 lead and iron; and said laxatives are used chronically.